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10/700,632	11/05/2003	Mary G. Hoffee	A-8427	8127

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,632	HOFFEE ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60 and 62-71* is/are pending in the application.

4a) Of the above claim(s) *33-58 and 63-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32, 59-60 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claim 61 is cancelled.

Claims 1-2, 59-60 and 62 have been amended.

2. Claims 33-58 and 63-71 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claims 1-32, 59-60 and 62 are under consideration.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This Office Action contains New Grounds of Rejections.

Objections/Rejections Withdrawn

6. The objection to the abstract for using the legal phraseology "said antibodies" is withdrawn in view of the newly submitted abstract filed 11/14/2006.

7. The objection to the disclosure as containing embedded hyperlinks and/or other form of browser-executable code is withdrawn in view of the amendments to the specification filed 11/14/2006.

8. The objection to the specification as disclosing "5 ?" and disclosing "derives from the mouse IgV? 8-27 germline" is withdrawn in view of the amendments to the specification filed 11/14/2006.

9. The objection to the Brief Description of the Drawings for Figures 8A and 8B as lacking sequence identifiers is withdrawn in view of the amendment to the Brief Description of the Drawings for Figures 8A and 8B filed 11/14/2006.

10. The objection to the specification is the use of the trademark Titertek® is withdrawn in view of the amendments to the specification field 11/14/2006.

11. The rejection of claims 59-60 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "improved antibody or epitope binding fragment thereof" is withdrawn in view of the amendments to the claims.

12. The rejection of claims 1-2 and 61 under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims is withdrawn in view of the amendments to the claims and applicant's arguments.

13. The rejection of claims 1-8, 15 and 17-28 under 35 U.S.C. 102(b) as being anticipated by R & D Focus Drug News, 12 November 2001, as evidenced by the specification is withdrawn in view of applicants arguments that the publication date of the reference is less than one year before Applicants' priority date and in view of the Declaration under 37 CFR 1.132 filed 11/14/2006, providing evidence that the My9-6 antibody is the work of the inventors and not the work of "another" as required under 35 U.S.C. 102(a).

14. The rejection of claims 1-8, 15 and 17-28 under 35 U.S.C. 102(a) as being anticipated by Lutz et al (Proceedings of the American Association for cancer research Annual Meeting, Vol. 43, p. 912, March 2002) or Goldmacher et al (Proceedings of the American Association for cancer research Annual Meeting, Vol. 43, p. 254, March 2002), as evidenced by the specification is withdrawn in view of the Declaration under 37 CFR 1.132 filed 11/14/2006, providing evidence that the My9-6 antibody is the work of the inventors and not the work of "another" as required under 35 U.S.C. 102(a).

15. The rejection of claims 17-32 under 35 U.S.C. 103(a) as being unpatentable over Goldenberg et al (U.S. Patent 6,759,045 B2, 8/8/2000) in view of R & D Focus Drug News, 12 November 2001, as evidenced by the specification is withdrawn in view of applicants arguments that the publication date of the reference is less than one year before Applicants' priority date and in view of the Declaration under 37 CFR 1.132 filed 11/14/2006 providing evidence that the My9-6 antibody is the work of the inventors and not the work of "another".

Response to Arguments

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. The rejection of claims 3-14, 17-32, 59-60 and 62 and newly applied to claims 15-16 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated antibodies and epitope-binding fragments thereof that specifically bind CD33 and comprise the heavy chain CDRs of SEQ ID Nos:1-3 and the light chain CDRs of SEQ ID Nos:4-6 or comprises the heavy chain variable region of SEQ ID NO:7 and/or the light chain variable region of SEQ ID NO:8 or comprising the heavy chain variable region of SEQ ID NO:9 and/or the light chain variable region of SEQ ID NO:10 as well as conjugates thereof and compositions comprising said isolated anti-CD33 antibodies or epitope-binding fragments thereof, does not reasonably provide enablement for all of the embodiments embraced by the claims is maintained and made again.

The response filed 11/14/2006 states that the specification exemplifies an isolated antibody that binds to CD33. The isolated antibody was sequenced and humanized, and was determined to have heavy chain variable region sequences set forth in SEQ ID Nos:7 (murine) and 9 (humanized), and light chain variable region sequences which are set forth in SEQ ID Nos:8 (murine) and 10 (humanized). According to applicant the specification also exemplifies functional equivalents of these antibodies (such as homologues, and mutants with deletions and insertions) produced through changes within the variable and/or constant region sequences that flank a particular set of CDRs (par. 91) or in the CDRs themselves (par. 97). The specification teaches that procedures for making antibody homologues and mutants is routine in the art, and provides an assay for determining binding activity of the antibody to CD33. Applicant states that the claims recite homologues having homology to only the variable regions of the heavy and light chains, thus the genus of homologs recited in the claims

is limited to a small well-defined genus, only encompassing homologues of four specific sequences – SEQ ID Nos:7-10. Applicant argues that in addition, Figures 16A and B provide specific examples of humanized sequence homologs of the variable region sequences of the light and heavy chains and the humanized My9-6 antibodies can compete equally well for CD33 binding as murine My9-6 antibody. Applicant points to paragraph [97] of the specification which includes citations to a number of publications that teach how amino acid changes at various positions of the CDR regions of the antibody sequence can be made. Finally, applicant notes that Examples 2 and 3 of the specification provide a detailed explanation of how specific amino acids that were used to replace the murine My9-6 antibody variable region surface residues were chosen, as well as a detailed explanation of the methods used to construct, test and use the homologs.

Applicants' arguments have been fully considered but are not found persuasive. The claims are drawn to an antibody or epitope-binding fragment thereof that specifically binds CD33 and comprises a heavy chain variable region comprising an amino acid sequence that is represented by SEQ ID NO:7 or 9 or comprises a light chain variable region comprising an amino acid sequence that is represented by SEQ ID NO:8 or 10 as well as sequences that are at least 90% identical to said heavy and light chain sequences. Thus, the claim language reads upon fragments of a variable region or even fragments of a single CDR since two amino acids of SEQ ID NO:7, for example, is merely one interpretation of "an amino acid sequence" represented by SEQ ID NO:7. Additionally, the claims encompass sequences that are at least 90% identical to the variable region or CDR fragments. Hence, in contrast to applicants' arguments that the claims are drawn to a limited, well-defined genus, the claims are drawn to a broad genus of antibodies that contain fewer than all six CDRs, three from the heavy chain and three from the light chain and do not bind antigen. Applicant refers to the murine My9-6 antibody sequences (i.e., SEQ ID Nos:7 and 8) and argues with the humanized My9-6 sequences (i.e., SEQ ID Nos:9 and 10) as being exemplary homologues of the recited sequences, however, in both cases the antibodies comprise all six CDRs, three from the heavy chain and three from the light chain in their proper

order and in the context of framework sequences which maintain their correct spatial orientation have the requisite CD33 binding function. Further, the claims are drawn to sequences that are 90% identical to applicant's exemplary embodiment, humanized My9-6. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970).

With respect to applicants' arguments that the specification provides procedures for making antibody homologues and mutants is routine in the art and applicants description of including citations to a number of publications that teach how amino acid changes at various positions of the CDR regions can be made. While the art does teach methods of making antibody homologues and mutants by routine experimentation, it is not routine nor predictable in the art which residues in a givn variable domain are necessary for binding antigen and which residues are tolerant to change. Again, the claims are drawn to a broad genus of variant variable domain sequences and fragments thereof, which are responsible for the antigen-binding function of the antibody. Paul provides evidence that the amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin and Rudikoff et al and Coleman (cited on PTO-892 mailed 6/14/06) illustrates the unpredictability in the art as far as alterations in the residues of a CDR and the effect on antigen binding. Patti et al (US 2005/0287164 A1) further exemplifies the unpredictability pertaining to the claimed sequences that are at least 90% identical to the recited heavy or light chain variable region sequences. Patti shows an antibody (monoclonal antibody 12-9) comprising a VL sequence that is 93% identical to the instantly claimed VL sequence of SEQ ID NO:8 and the antibody does not bind CD33. Further, claims 59-60 and 62 are very broad encompassing anti-CD33 antibodies having any number of mutations, deletions or insertions in the variable domains, broadly encompassing CDR deletions. The only evidence in the record is that all six CDRs of the My9-6 antibody (i.e., SEQ ID Nos:1-6) are required for binding CD33. Applicant's arguments that the specification teaches how to make homologues, and references a large number materials that teach how changes can be made, thus providing the skilled

artisan with the tools to make and test homologues is merely an invitation for those skilled in the art to figure out for themselves what the sequences look like and which antibody variants may have the requisite CD33 binding function and affinity, which is insufficient to constitute adequate enablement. In short, the instant application describes methods for determining whether a given antibody variant possesses the claimed characteristics, and identifies some broad categories that *might work*, however, these descriptions, without more precise guidelines, amount to little more than "a starting point, a direction for further research." *Genentech*, 108 F.3d at 1366. *See also Calgene*, 188 F.3d at 1374 ("the teachings set forth in the specification provide no more than a 'plan' or 'invitation' for those of skill in the art to experiment practicing [the claimed invention]; they do not provide sufficient guidance or specificity as to how to execute that plan"); *National Recovery Technologies*, 166 F.3d at 1198 (stating that patent-in-suit "recognizes a specific need... and suggests a theoretical answer to that need. It provides a starting point from which one of skill in the art can perform further research in order to practice the claimed invention, but this is not adequate to constitute enablement"). The instant specification does not describe the claimed invention in terms that will "enable any person skilled in the art... to make and use" the invention commensurate in scope with the claims. At most, the specification will enable a person of ordinary skill in the art to attempt to discover how to practice the claimed invention. "(A) specification which describes' does not necessarily also enable' one skilled in the art to make or use the claimed invention." See *In re Armbruster*, 512 F.2d 676, 677, 185 USPQ 152, 153 (CCPA 1975).

Although the specification does provide information as to how to identify which sites to mutate, the specification does not demonstrate which residues can predictably be substituted and result in an antibody that has the claimed properties including increased affinity for the CD33. It would require undue experimentation to identify which residues to substitute or which residues when substituted would likely result in an antibody specific for CD33 with increased affinity. Further, as discussed supra, the scope of the claims are much broader than Examples 2 and 3 of the specification, which are limited to humanized My9-6 antibodies where most of the mutations occur at

framework residues identified as interacting with the CDRs or directly with antigen and their maintenance is required for antigen binding.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed antibodies in a manner reasonably correlated with the scope of the claims, broadly including less than all six CDRs of mouse monoclonal antibody My9-6 (i.e., SEQ ID Nos:1-6), or comprising a heavy and/or light chain variable region(s) having "an amino acid sequence" represented by SEQ ID NO:7 and/or 9, or represented by SEQ ID NO:8 and/or 10, respectively, or having "an amino acid sequence" that is 90-95% identical to SEQ ID Nos:7 and/or 8, or 90-95% identical to SEQ ID Nos:9 and/or 10, respectively, or improved antibodies comprising any number of amino acid substitutions, deletions or insertions in the variable regions of SEQ ID Nos:7 and/or 8 or SEQ ID Nos:9 and/or 10. Without such guidance, the changes which can be made in the protein's structure and still maintain antigen-binding function is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F, 2d 1200, 18 USPQ 1016 (Fed. Cir. 1991) at 18 USPQ 1026 1027 and Ex parte Forman, 230 USPQ 546 (BPAI 1986).

In view of the lack of the predictability of the art to which the invention pertains as evidenced by Paul W. E., Rudikoff et al, Coleman, and Patti et al, the lack of guidance and direction provided by applicant, and the absence of working examples, undue experimentation would be required to practice the claimed antibodies, or antibodies comprising just any mutations, deletions or insertions wherein the antibodies bind CD33 or have increased affinity for CD33 with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed antibodies and absent working examples providing evidence which is reasonably predictive that the claimed antibodies bind CD33, commensurate in scope with the claimed invention.

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. The rejection of claims 1-8 and 15 under 35 U.S.C. 102(b) as being anticipated by Weitzhandler et al (Journal of Pharmaceutical Sciences, 83(12):1670-1675, December 1994) as evidenced by the specification is maintained.

The response filed 11/14/2006 states that Weitzhandler et al do not specifically teach the antigen to which the My9-6 antibody binds and as a result, Weitzhandler et al is not sufficiently enabling citing MPEP 2121.01 for support. Applicant states that Weitzhandler et al does not characterize the My9-6 antibody nor disclose any binding activity and as such would not enable a skilled artisan to use the publication's description of the antibody to make the claimed invention without undue experimentation. Applicant also argues that the My9-6 antibody of the present invention was not deposited in the ATCC until November 7, 2002 and therefore, the antibody was not publicly available as of the 1994 publication date of Weitzhandler. Applicants' arguments have been fully considered but are not found persuasive. The examiner acknowledges that in the absence of the antigen to which the My9-6 antibody binds and in view of the lack of characterization of the My9-6 including the absence of any sequence disclosure of the My9-6 antibody, that mere naming of the My9-6 antibody does not provide an enabling disclosure unless the My9-6 was made publicly available. With respect to the availability of the My9-6 antibody and as acknowledged by Applicant, Weitzhandler teaches that the antibody was obtained from Immunogen, Inc., the assignee of the instant application (3rd par. Col. 2, pg. 1670), providing strong evidence that the My9-6 antibody was made publicly available. Applicant is reminded that when the reference relied on expressly anticipates all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of

operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP 716.07. Applicant has not provided any facts sufficient to rebut the presumption of operability and as noted by Applicant Weitzhandler provide strong evidence that the My9-6 antibody was made publicly available. Applicant is reminded that the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Applicants' arguments regarding the deposit of the My9-6 antibody and applicants statement that the antibody was not publicly available as of the 1994 publication date of Weitzhandler is acknowledged, however, there is no factual support for applicants' statement that the My9-6 antibody was not available prior to the deposit in the ATCC on November 7, 2002. Further, applicants' statement that the antibody was not publicly available as of the 1994 publication date of Weitzhandler is curious in view of the evidence of Weitzhandler that the antibody was provided by the assignee, Immunogen, Inc.

Thus, the rejection of claims 1-8 and 15 under 35 U.S.C. 102(b) as being anticipated by Weitzhandler et al as evidenced by the specification is maintained.

20. The rejection of claims 1-8, 15 and 17-28 under 35 U.S.C. 102(b) as being anticipated by CML NewsBytes, 10/24/2001, (www.cmlsupport.com/cmlnewsbytesarchives2.htm), as evidenced by the specification is maintained.

The response filed 11/14/2006 states that CML NewsBytes merely provides the name of a drug, and does not indicate that whether the named drug comprises an antibody nor does it provide any information regarding the identity of the antigen to which the drug binds. As a result, CML NewsBytes is not sufficiently enabling to serve as prior art citing MPEP 2121.01 for support. Applicant states that CML NewsBytes does not characterize the My9-6 antibody nor disclose any binding activity and as such would not enable a skilled artisan to use the publication's description of the drug to make the claimed invention without undue experimentation. Applicant also argues that the My9-6 antibody of the present invention was not deposited in the ATCC until

November 7, 2002 and therefore, the antibody was not publicly available as of the 2001 publication date of CML NewsBytes. Applicants' arguments have been fully considered but are not found persuasive. The examiner acknowledges that in the absence of the antigen to which the My9-6 antibody binds and in view of the lack of characterization of the My9-6 including the absence of any sequence disclosure of the My9-6 antibody, that mere naming of the My9-6 antibody does not provide an enabling disclosure unless the My9-6 was made publicly available. However, applicant is reminded that when the reference relied on expressly anticipates all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). See also MPEP 716.07. Applicant has not provided any facts sufficient to rebut the presumption of operability. Applicant is reminded that the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Applicants' arguments regarding the deposit of the My9-6 antibody and applicants statement that the antibody was not publicly available as of the 2001 publication date of CML NesBytes is acknowledged, however, there is no factual support for applicants' statement that the My9-6 antibody was not available prior to the deposit in the ATCC on November 7, 2002. Further, applicants' statement that the antibody was not publicly available as of the 2001 publication date of CML NewsBytes is curious in view of the evidence of record (e.g., Weitzhandler et al, 3rd par. Col. 2, pg. 1670) that the antibody was provided by the assignee, Immunogen, Inc, 8 years prior to the deposit in the ATCC.

Thus, the rejection of claims 1-8, 15 and 17-28 under 35 U.S.C. 102(b) as being anticipated by CML NewsBytes as evidenced by the specification is maintained.

New Grounds of Objections/Rejections

21. Claims 3-14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in

proper dependent form, or rewrite the claims in independent form. Base claim 2, recites an anti-CD33 antibody comprising a heavy chain variable region comprising the CDRs of SEQ ID Nos: 1-3 and a light chain variable region comprising the CDRs of SEQ ID Nos:4-6. As depending from base claim 2, claims 3-4 and 9-10 recite wherein the heavy chain variable region has at least 90% and 95% sequence identity to an amino acid sequence represented by SEQ ID NO:7 or 9 and claims 6-7 and 12-13 recite wherein the light chain variable region has at least 90% and 95% sequence identity to an amino acid sequence represented by SEQ ID NO:8 or 10. Thus, claims 3-4, 6-7, 9-10 and 12-13 embrace heavy and light chain variable regions that do not comprise the CDRs recited in base claim 2, i.e., the CDRs may comprise amino acid substitutions, deletions or insertions. Further, dependent claims 5, 8, 11 and 14 are drawn to antibodies that comprise "an amino acid sequence" of the recited heavy and light chain variable regions, which encompasses fragments of the recited variable regions as few as two amino acids and as such does not include the CDRs recited in base claim 2. Any claim which is in dependent form but which is so worded that it, in fact is not, as, for example, it does not include every limitation of the claim on which it depends, will be required to be canceled as not being a proper dependent claim; and cancellation of any further claim depending on such a dependent claim will be similarly required.

22. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

23. Claims 1-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The claims are indefinite in the recitation "represented by..." because it is unclear what is contemplated by the phrase. The phrase "represented by" renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Amending the claims to recite

"comprising the amino acid sequence of SEQ ID NO:X", for example, would overcome this rejection.

b. Claims 4, 7, 10 and 13 recite the limitation "said amino acid". There is insufficient antecedent basis for this limitation in the claim. Base claim 2 from which claims 4, 7, 10 and 13 depend only recites heavy and light chain CDR sequences and it is unclear what variable region sequence is being referenced in the claims. For example, claim 4 recites that said heavy chain variable region has at least 90% sequence identity to said amino acid sequence represented by SEQ ID NO:7, however, base claim 2 does not recite "said amino acid sequence represented by SEQ ID NO:7". Is the heavy chain variable region 90% identical to the recited CDRs of base claim 2 or 90% identical to SEQ ID NO:7 or is some other meaning contemplated by the phrase?

c. Claims 19-20 are indefinite for reciting "derivatives thereof". The claims are indefinite for reciting "derivatives" as the exact meaning of the word is not known. The term "derivatives" is not one, which has a universally accepted meaning in the art nor is it one which has been adequately defined in the specification. The primary deficiency in the use of this phrase is the absence of an ascertainable meaning for said term. Since it is unclear as to the nature, direction and extent to which the drugs and prodrugs are to be derivatized to yield the class of derivatives referred to in the claims, there is no way for a person of skill in the art to ascribe a discrete and identifiable class of compounds to said term. In absence of a single defined art recognized meaning for the term and lacking a definition of the term in the specification, one of skill in the art could not determine the metes and bounds of the claims.

24. Claims 1-8, 15 and 17-28 under 35 U.S.C. 102(b) as being anticipated by BioCentury Part II; vol. 9, No. 48, pp. B1-B22, October 29, 2001, as evidenced by the specification.

BioCentury Part II teach murine monoclonal antibody My9-6 linked to the maytansinoid drug DM1 (see pg. B13, 2nd col.), wherein monoclonal antibody My9-6 is identical to the claimed murine monoclonal antibody My9-6 comprising the heavy and light chain variable regions of SEQ ID Nos:7 and 8, respectively, inclusive to the CDRs of SEQ ID Nos:1-6 as evidence by the specification (see Figs 8A and 8B and Example 4). Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Accordingly, murine monoclonal antibody My9-6 taught by BioCentury Part II necessarily comprises the heavy chain variable region of SEQ ID NO:7 and the light chain variable region of SEQ ID NO:8 and binds CD33. Further,

given that that My9-6-DM1 immunoconjugate was shown to eliminate tumors in mice, one of ordinary skill in the art would readily envisage that the administered My9-6-DM1 immunoconjugate was necessarily present in a composition or pharmaceutical composition comprising a pharmaceutically acceptable agent.

Thus, BioCentury Part II anticipates the claims as evidenced by the specification.

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

26. Claims 1-8, 15 and 17-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldenberg et al (U.S. Patent 6,759,045 B2, 8/8/2000, cited on PTO-892 mailed 6/14/06) in view of BioCentury Part II, vol. 9, No. 48, pp. B1-B22, October 29, 2001, as evidenced by the specification.

The claims are being interpreted as drawn to the murine monoclonal antibody My9-6 comprising the heavy chain CDRs of SEQ ID Nos:1-3 and the light chain CDRs of SEQ ID Nos:4-6, wherein the My9-6 antibody is linked to a drug or prodrug as recited in claims 19-20 or wherein said My9-6 antibody or immunoconjugate thereof is present in a composition or pharmaceutical composition comprising a pharmaceutically acceptable agent as well as a diagnostic reagent comprising the My-9-6 antibody that is labeled with a biotin label, an enzyme, a radio-label, a fluorophore, a chromophore, an imaging agent or a metal ion.

Goldenberg et al teach antibodies and immunoconjugates thereof for the treatment of leukemia, wherein the immunoconjugates comprise a drug, including calicheamicin or is labeled with a fluorescent or chromogenic agent for detection as well as pharmaceutical compositions comprising the antibodies or immunoconjugates thereof and a pharmaceutically acceptable carrier (see entire document, particularly columns 13-15 and 17). Goldenberg et al do not specifically teach presently claimed antibody or conjugates thereof or compositions comprising such. These deficiencies are made up for in the teachings of BioCentury Part II.

BioCentury Part II teaches the My9-6 antibody for targeting myeloid leukemia cells and when conjugated to the maytansinoid drug DM1, completely eliminated tumor xenografts in mice (see pg. B13, 2nd col.). As evidenced by the specification, the My9-6 antibody necessarily comprises the heavy and light chain variable regions of SEQ ID Nos:7 and 8, respectively, inclusive to the CDRs of SEQ ID Nos:1-6 as evidence by the specification (see Figs 8A and 8B and Example 4).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have conjugated the My9-6 antibody as taught by BioCentury Part II with the various chemotherapeutic drugs (i.e., calicheamicin) or detectable labels of Goldenberg et al as well as produce pharmaceutical compositions

comprising the My9-6 antibody or conjugates thereof and a pharmaceutically acceptable carrier for therapeutic benefit in leukemia patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have to have conjugated the My9-6 antibody as taught by BioCentury Part II with the various chemotherapeutic drugs (i.e., calicheamicin) or detectable labels of Goldenberg et al as well as produce pharmaceutical compositions comprising the My9-6 antibody or conjugates thereof and a pharmaceutically acceptable carrier for therapeutic benefit in leukemia patients because Goldenberg et al teach antibodies and immunoconjugates thereof for the treatment of leukemia, wherein the immunoconjugates comprise a drug, including calicheamicin or is labeled with a fluorescent or chromogenic agent for detection as well as pharmaceutical compositions comprising the antibodies or immunoconjugates thereof and a pharmaceutically acceptable carrier and BioCentury Part II teaches the My9-6 antibody linked to the maytansinoid drug DM1 that effectively inhibited tumor xenografts in mice and as evidenced by the specification the My9-6 antibody of the prior art is identical to the claimed murine monoclonal antibody My9-6 and necessarily comprises the heavy and light chain variable regions of SEQ ID Nos:7 and 8, respectively, inclusive to the CDRs of SEQ ID Nos:1-6. Therefore, given the success of the My9-6 antibody in the treatment of tumor xenografts in mice, one of ordinary skill in the art would have been motivated to conjugate the My9-6 antibody to other suitable chemotherapeutic agents, which were known to those of skill in the art (see col. 14, lines 44-55 of Goldenberg) or conjugate the My9-6 antibody to a detectable label for diagnosis and administer the My-9-6 antibody or conjugates thereof in a pharmaceutically acceptable carrier in leukemia patients for therapeutic benefit. Thus, there would be advantages to conjugating the My9-6 antibody to the various therapeutic and diagnostic agents and the inclusion of a pharmaceutically acceptable carrier facilitates administration in leukemia patients. Thus, it would have been *prima facie* obvious to one skilled in the art to have conjugated the My9-6 antibody with various chemotherapeutic drugs (i.e., calicheamicin) or detectable labels as well as produce pharmaceutical compositions comprising the My9-6 antibody or conjugates thereof and

a pharmaceutically acceptable carrier for therapeutic benefit in leukemia patients in view of Goldenberg et al and Biocentury Part II.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

27. No claims are allowed.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1643

DB
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